UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,581	06/23/2003	Michelle M. Hanna	2072.0010002	8564

26111 7590 06/14/2006

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,581	HANNA, MICHELLE M.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-84,106-111,113,114,130-136 and 138-148* is/are pending in the application.

4a) Of the above claim(s) *72-84,106-111,131-133 and 136-148* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55-71,113,114,130-135,138-140 and 142-148* is/are rejected.

7)☒ Claim(s) *131-133,135 and 142-144* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/23/06, 10/10/03*; 8/13/03 10/10/03 12/13/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: ~~IDS rec'd 12/23/04~~ ~~8/13/03~~

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 55-71, 113, 114, 130-135, and 138-148 in the reply filed on April 20, 2006 is acknowledged. The traversal is on the ground(s) that Inventions of I, II, and IV have been classified in the same class and subclass. Based on this, Applicants assert that the search results from Invention I would result in the identification of art relevant to Inventions II and IV. This is not found persuasive because Applicants cannot rely on the fact that the invention was classified under the same class and subclass for justifying undue search burden. The inventions of I, II, and IV were classified under class 435, subclass 6. Inventions which are classified under this large class are, for example, nucleic acid sequencing, diagnostic regarding expression of nucleic acids, mutations, any assays involving nucleic acid hybridization, amplification (in part), nucleic acids comprising mutations, etc. Hence, were one to assert that all these invention should be searched together without serious search burden solely based on the fact that they are all classified under the same class and subclass would be flawed. Clearly, a search regarding a diagnosis based on mutation would be different from a search regarding a diagnostic based on the expression level of the nucleic acid markers, though classified in the same classification. Even within the confines of the same mutation detection, a search regarding a particular phenotype based on a mutation would be different from a search regarding a different phenotype based on a mutation. Simply put, an argument solely based on the classification and subclass, absent other convincing supporting arguments, cannot substantiate Applicants' position that search burden is not undue.

The requirement is still deemed proper and is therefore made FINAL.

Claims 72-84, 106-111, 131-133, 135, 137-140, 142-148 are withdrawn (in-part)[1] from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 20, 2006.

Applicants are advised that claims 136 and 141 are wholly withdrawn from further consideration as being drawn to nonelected invention. Claim 141 is dependent from claim 136. Claim 136 belongs to Invention of Group IV. Thus, claims 136 and 141 are not part of the elected invention.

Information Disclosure Statement

The IDS received on June 23, 2003; August 12, 2003; October 10, 2003; and December 23, 2004 are acknowledged..

Their signed PTO-1449 are enclosed herewith.

Drawings

The drawings received on June 23, 2003 and seven sheets of drawings received on November 10, 2005 are acceptable.

Sequence Compliance

The application contains several Figures which recite nucleotide sequences which must comply with rules set forth in 37 CFR 1.821 through 1.825. For example, Figure 29A discloses a nucleotide sequence having a sequence of more than 10 contiguous nucleotides without a proper SEQ ID identifier.

---

[1] Claims 131-133, 135, 138-148 are multiple dependent claims depending from different independent claims which are patentably distinct. Therefore, these claims are withdrawn from further prosecution with respect to their dependencies on the patentably distinct inventions of Inventions II-IV.

A fully responsive amendment must contain response to all objections/rejections made herein, a CRF (computer readable medium), a paper copy of the sequence listing, a statement under 37 CFR 1.821(f).

Claim Objections

Claims 131-133 and 135 are objected to for being dependent on withdrawn claims 72 and 106 (i.e., non-elected invention)[2].

Claims 142-144 are objected to for being dependent on withdrawn claim 141.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 63, 70, 71, 114, 131-133, 135, 138-140, and 142-148 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 63 recites the limitation, "said chain terminator."

There is insufficient antecedent basis for this limitation in the claim with respect to its dependency on claims 55 and 56.

Claim 70 recites the limitation, "said target pathogen polynucleotide."

There is insufficient antecedent basis for this limitation in the claim with respect to its dependency on claim 55.

---

[2] Claims 131-133 and 135 are multiple dependent claims which are dependent on elected inventions as well as non-elected invention. Thus claims are examined to the extent of their dependency on the elected invention.

Claim 71 is indefinite for reciting the phrase, "hybridizing a single stranded target polynucleotide," in step (b). Steps (a) and (b) of claim 71 recites that a capture probe is hybridized with a target polynucleotide in the test sample. Thus, the above-recited phrase which states, "hybridizing a single stranded target polynucleotide," becomes indefinite in whether a single-stranded target polynucleotide is the same target polynucleotide which is hybridized to the capture probe or an entirely different target polynucleotide.

For the purpose of compact prosecution, the former interpretation is assumed.

Claims 131-133, 135, 138-140, and 142-148 are indefinite by way of their dependency on claim 71.

Claim 114 is indefinite because the claim is recited as "further comprising" steps (a) and (b). It becomes indefinite whether steps (a) and (b) is to replace the steps (a) and (b) of the parent claim 113, or the steps are supposed to be conducted previously to the steps of claim 113, or the steps are supposed to be conducted after the steps of claim 113.

Claim 138 is a multiple dependent claim which contain self-dependency. It is indefinite what limitation is being incorporated by its dependency.

Claim 147 recites the limitation, "the RNA-dependent RNA polymerase." There is insufficient antecedent basis for this limitation in the claim with respect to its dependency on claims 55, 56, 71, and 113.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 55, 57-59, 61-68, 70, and 131-135 are rejected under 35 U.S.C. 102(b) as being anticipated by Sasaki et al. (PNAS USA, March 1998, vol. 95, pages 3455-3460; IDS reference).

Sasaki et al. disclose a transcriptional sequencing method, said method comprising the steps:

a) hybridizing a single stranded target polynucleotide with an abortive promoter cassette comprising a sequence that hybridizes to the a single-stranded target polynucleotide, and a region that can be detected by transcription by a polymerase (Figure 4, see primer comprising a sequence complementary to the target nucleic acid, and a region which is a T7 promoter or T3 promoter, which is recognized by a polymerase);

b) incubating said target polynucleotide with an RNA polymerase (with T7 or T3 RNA polymerase; see Figure 4), an initiator (or 1mM GMP; see page 3456, 2nd column, bottom paragraph) and a terminator (fluoresecent dye terminator; see page 3457, 1st column, bottom paragraph);

c) synthesizing oligonucleotide transcripts that is complementary to the initiation start site of the abortive promoter cassette, until dye terminator is incorporated in to the transcription product (see page 3457, Figure 4);

d) detecting the oligonucleotide transcripts by electrophoresis sequencing method (see Figure 5; page 3460, 1st column).

The limitation, "abortive promoter sequence" is not specifically defined by the instant specification what is considered to be an "abortive promoter cassette," and since the claim does not recite a structure of such a cassette, based on a reasonable broadest interpretation of the claim, any structure which comprises promoter sequence that is capable of effecting abortive reiterative synthesis, is deemed to meet this limitation, there by clearly anticipating claim 55.

With regard to claims 57-59, 64, and 134, the detection is achieved by the use of a modified nucleotide (fluorescent dye terminator; *see* page 3460, 1st column), particularly tetramethyl rhodamine (or TMR) (page 3456, Figure 2).

With regard to claims 61 and 62, the RNA polymerase is a T7 or T3 RNA polymerase (Figure 4; page 3455, 2nd column, bottom paragraph).

With regard to claim 63, the transcripts being produced would be met by the transcripts produced by Sasaki et al.

With regard to claims 65, 68, 135, the initiator is at least one nucleotides in length (dNTPs).

With regard to claim 66, the single-stranded target polynucleotide is DNA (page 3456, 2nd column, 2nd paragraph).

With regard to claim 67, one of the nucleotides are dUTP (page 3456, 1st column).

With regard to claim 70, the primer comprising the T7 or T3 promoter sequence has at least one nucleotide which hybridizes to the single-stranded target polynucleotide. Since the term, "linker" does not preclude a nucleotide, the primer of Sasaki et al. would anticipate this limitation.

With regard to claims 131-133, the primer of Sasaki et al. comprises nucleotide sequences which are complementary to the target polynucleotide. Whether such sequences would form a bubble complex or not, it is asserted that when an RNA polymerase binds to said region, a bubble formation would occur (as in any transcription reaction).

Therefore, Sasaki et al. clearly anticipate the invention as claimed.

Applicants are advised that amending the claims to clearly recite the structure of the "abortive promoter cassette" as exemplified in Figure 19 would overcome the instant rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 56, 57-71, 113, 114, 130-135, 138-140, and 142-148 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sasaki et al. (PNAS USA, March 1998, vol. 95, pages 3455-3460; IDS reference) in view of Kang et al. (U.S. Patent No. 6,268,131, issued July 31, 2001).

Sasaki et al. disclose a transcriptional sequencing method, said method comprising the steps:

a) hybridizing a single stranded target polynucleotide with an abortive promoter cassette comprising a sequence that hybridizes to the a single-stranded target polynucleotide, and a region that can be detected by transcription by a polymerase (Figure 4, see primer comprising a sequence complementary to the target nucleic acid, and a region which is a T7 promoter or T3 promoter, which is recognized by a polymerase);

b) incubating said target polynucleotide with an RNA polymerase (with T7 or T3 RNA polymerase; see Figure 4), an initiator (or 1mM GMP; see page 3456, 2nd column, bottom paragraph) and a terminator (fluoresecent dye terminator; see page 3457, 1st column, bottom paragraph);

c) synthesizing oligonucleotide transcripts that is complementary to the initiation start site of the abortive promoter cassette, until dye terminator is incorporated in to the transcription product (see page 3457, Figure 4);

d) detecting the oligonucleotide transcripts by electrophoresis sequencing method (see Figure 5; page 3460, 1st column).

The limitation, "abortive promoter sequence" is not specifically defined by the instant specification what is considered to be an "abortive promoter cassette," and since the claim does not recite a structure of such a cassette, based on a reasonable broadest interpretation of the claim, any structure which comprises promoter sequence that is capable of effecting abortive reiterative synthesis, is deemed to meet this limitation.

Sasaki et al. do not explicitly disclose that their method would be used in the detection of pathogens in a sample, such as RNA virus, or that an RNA dependent RNA polymerase is used for the transcription, or that the RNA dependent RNA polymerase is a poliovirus RNAP.

Kang et al. disclose a method of sequencing nucleic acid via use of RNA dependent RNA polymerases (column 9, lines 16-35 and 43-57), wherein the transcription of the template is initiated by a promoter sequence. An embodiment of the teachings of Kang et al. is drawn to the hybridization of the target nucleic acid to a primer which comprises a promoter sequence, wherein said primer is immobilized on a solid surface.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to apply the teachings of Sasaki et al. with the teachings of Kang et al. for the purpose of detection/characterizing pathogens (such as RNA virus) in a sample, for the well known benefit of survival of mankind.

Such benefit is clearly implied by Sasaki et al., wherein the artisans explicitly state that their method would be useful in diagnostics, clinical diagnosis and genome sequencing. Clearly, one of ordinary skill in the art would have recognized that clinical diagnosis would undoubtedly include detection of pathogens in clinical samples. Therefore, one of ordinary skill in the art would have been motivated to combine the teachings of Sasaki et al. with the teachings of Kang et al. so as to detect pathogens such as RNA-based pathogens. One of ordinary skill in the art at the time the

invention was made would have had a reasonable expectation of success at producing the combination since both teachings relied on the template nucleic acid having a promoter sequence which is recognized by the RNA dependent RNA polymerase to initiate the transcription reaction, wherein the transcription reaction is terminated by the incorporation of a terminating nucleotide, thereby rendering claims 56, 71, 113, 114, 130, 138-140, and 142-148 obvious.

With regard to claims 57-59, 64, and 134, the detection is achieved by the use of a modified nucleotide (fluorescent dye terminator; *see* page 3460, 1st column), particularly tetramethyl rhodamine (or TMR) (page 3456, Figure 2).

With regard to claims 61 and 62, the RNA polymerase is a T7 or T3 RNA polymerase (Figure 4; page 3455, 2nd column, bottom paragraph).

With regard to claim 63, the transcripts being produced would be met by the transcripts produced by Sasaki et al.

With regard to claims 65, 68, 135, the initiator is at least one nucleotides in length (dNTPs).

With regard to claim 66, the single-stranded target polynucleotide is DNA (page 3456, 2nd column, 2nd paragraph).

With regard to claim 67, one of the nucleotides are dUTP (page 3456, 1st column).

With regard to claim 70, the primer comprising the T7 or T3 promoter sequence has at least one nucleotide which hybridizes to the single-stranded target polynucleotide. Since the term, "linker" does not preclude a nucleotide, the primer of Sasaki et al. would anticipate this limitation.

With regard to claims 131-133, the primer of Sasaki et al. comprises nucleotide sequences which are complementary to the target polynucleotide. Whether such sequences would form a bubble complex or not, it is asserted that when an RNA polymerase binds to said region, a bubble formation would occur (as in any transcription reaction).

For the reasons discussed above, the invention as claimed is *prima facie* obvious over the cited reference.

Applicants are advised that amending the claims to clearly recite the structure of the "abortive promoter cassette" as exemplified in Figure 19 would overcome the instant rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 55-71, 113, 114, 130-135, 138-140, and 142-148 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 7,045,319. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the issued patents are narrower species of method which renders the broader claims of the instant application in a genus-species anticipatory way.

Claims 55-71, 113, 114, 130-135, 138-140, and 142-148 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26, 27, 103, 112, and 136-139 of copending Application No. 10/488,971 (herein, the '971 application). Although

the conflicting claims are not identical, they are not patentably distinct from each other because claims of the '971 application are narrower species of method which renders the broader claims of the instant application in a genus-species anticipatory way.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 55-71, 113, 114, 130-135, 138-140, and 142-148 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22, 32-34, and 44 of copending Application No. 10/976,240 (herein, the '240 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and the claims of the '240 application require the same method of reiteratively synthesizing oligonucleotide transcripts which are terminated, as well as employing an abortive promoter cassettes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 55-71, 113, 114, 130-135, 138-140, and 142-148 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-27 of copending Application No. 10/425,037. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of the instant application and the claims of the '240 application require the same method of reiteratively synthesizing oligonucleotide transcripts which are terminated, as well as employing an abortive promoter cassettes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 55-71, 113, 114, 130-135, 138-140, and 142-148 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over pending (and/or elected) claims of copending Application No. 10/600,045; 10/602,045; and 10/607,136. Although the conflicting claims are not identical, they are not patentably distinct from each other because as reasons already set forth above.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m. The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be

sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Primary Examiner
Art Unit 1637
6/12/2006

YOUNG J. KIM
PATENT EXAMINER

yjk